UNITED STATES DEPARTMENT OF COMMERCE United States Patent and Trademark Office Address: COMMISSIONER FOR PATENTS P.O. Box 1450 Alexandria, Virginia 22313-1450 www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/584,076	08/23/2006	Qing Dong	34060-US-PCT	8766
75074 7590 05/29/2008 NOVARTIS INSTITUTES FOR BIOMEDICAL RESEARCH, INC. 400 TECHNOLOGY SQUARE			EXAMINER	
			MOORE, SUSANNA	
CAMBRIDGE, MA 02139			ART UNIT	PAPER NUMBER
			1624	
			MAIL DATE	DELIVERY MODE
			05/29/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

	Application No.	Applicant(s)				
	10/584,076	DONG ET AL.				
Office Action Summary	Examiner	Art Unit				
	SUSANNA MOORE	1624				
The MAILING DATE of this communication app Period for Reply	ears on the cover sheet with the c	orrespondence address				
A SHORTENED STATUTORY PERIOD FOR REPLY WHICHEVER IS LONGER, FROM THE MAILING DA  - Extensions of time may be available under the provisions of 37 CFR 1.13 after SIX (6) MONTHS from the mailing date of this communication.  - If NO period for reply is specified above, the maximum statutory period w  - Failure to reply within the set or extended period for reply will, by statute, Any reply received by the Office later than three months after the mailing earned patent term adjustment. See 37 CFR 1.704(b).	ATE OF THIS COMMUNICATION 36(a). In no event, however, may a reply be time will apply and will expire SIX (6) MONTHS from cause the application to become ABANDONE	lely filed the mailing date of this communication. (35 U.S.C. § 133).				
Status						
1) Responsive to communication(s) filed on 25 Ma	arch 2008					
	action is non-final.					
3) Since this application is in condition for allowar		secution as to the merits is				
•	closed in accordance with the practice under <i>Ex parte Quayle</i> , 1935 C.D. 11, 453 O.G. 213.					
Disposition of Claims						
4)⊠ Claim(s) <u>1-103</u> is/are pending in the application.						
4a) Of the above claim(s) <u>43-49 and 54-94</u> is/are withdrawn from consideration.						
5) Claim(s) is/are allowed.						
6)⊠ Claim(s) <u>1-42,50-53 and 95-103</u> is/are rejected.						
7) Claim(s) is/are objected to.						
8) Claim(s) are subject to restriction and/or	election requirement.					
Application Papers	•					
9)☑ The specification is objected to by the Examine 10)☐ The drawing(s) filed on is/are: a)☐ acce		Evaminor				
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).						
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).						
11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.						
Priority under 35 U.S.C. § 119						
<ul> <li>12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).</li> <li>a) All b) Some * c) None of:</li> <li>1. Certified copies of the priority documents have been received.</li> <li>2. Certified copies of the priority documents have been received in Application No</li> <li>3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).</li> <li>* See the attached detailed Office action for a list of the certified copies not received.</li> </ul>						
Attachment(s)  1) Notice of References Cited (PTO-892)  4) Interview Summary (PTO-413)						
1) X Notice of References Cited (PTO-892) 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)	(PTO-413) ite					
3) 🗖 Information Disclosure Statement(s) (PTO/SB/08)	atent Application					
Paper No(s)/Mail Date <u>6/22/06</u> . 6) Other:						

#### **DETAILED ACTION**

#### Election/Restrictions

Applicant's election without traverse of Group I in the reply filed on 3/25/2008 is acknowledged. Group I, drawn to pyrazolo[3,4-d]pyrimdines and simple compositions thereof, embraced by claims 1-42, 50-53 and 95-105 was elected by Applicant. Applicant has not pointed to any errors in the Examiners analysis of the classification of the different inventions. The requirement is deemed proper and is therefore made **FINAL**.

There are 103 claims pending and 57 under consideration. Claims 1-50, 53 and 95-105 are compound claims. Claims 51 and 52 are composition claims. Claims 53-94 are claims drawn to nonelected subject matter, which are currently withdrawn from consideration. This is the first action on the merits. The application concerns some pyrazolo[3,4-d]pyrimidine compounds and simple compositions thereof.

This application contains claims 1-35, 43-94 and 95-103, drawn to an invention nonelected without traverse in the paper of 3/25/2008. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

#### Information Disclosure Statement

The information disclosure statement filed 6/22/2006 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

# Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Substituted Pyrazolo[3,4-d]pyrimidines as Cytokine Modulators. This is just a suggestion. Please feel free to change the name to accurately describe the current invention.

# Claim Objections

Claim 1 is objected to because of the following informalities: replace the ... "CO<sup>2</sup>R<sub>6</sub>" with ... "CO<sub>2</sub>R<sub>6</sub>" on page 5, line 15. Appropriate correction is required.

Claim 1 is objected to because of the following informalities: replace "thiamorpholinyl" with "thiomorpholinyl" on page 6, line 14. Appropriate correction is required.

Claim 1 is objected to because of the following informalities: replace "alkysulfonyl" with "alkylsulfonyl" on page 7, line 5. Appropriate correction is required.

Claim 24 is objected to because of the following informalities: replace "pyrrazolopyrimidine" with "pyrazolopyrimidine" on page 8, line 2. Appropriate correction is required.

Claim 34 is objected to because of the following informalities: replace "CH2-heterocyclyl" with "CH<sub>2</sub>-heterocyclyl" on page 9, line 2. Appropriate correction is required.

Claim 53 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is

required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 1 does not further limit claim 1, since an intended use is not given patentable weight in a compound claim.

Claim 101 is objected to because of the following informalities: replace "azacinyl" with "azecinyl" on page 55, line 2. Appropriate correction is required.

# Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-42, 50-53 and 95-103 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The word "derivatives" is vague in claim 1. A derivative is a substance or compound obtained from, or regarded as derived from, another substance or compound. What are these "derivatives?" Are the "derivatives" covered by the scope of the genus of formula (I)?

The carbon in the formula "CR<sup>4</sup>cycloalkyl" is vague in claim 1, page 4, line 12; and claim 12, page 7, line 2. The valency of nitrogen is trivalent, not divalent. Thus, just a nitrogen atom at this position is not sufficient to maintain a neutral substituent at R3.

The carbon in the "NC" from the substituent "NR $^7$ C(=NC)(CR $^9$ R $^{10}$ )<sub>r</sub>R $^6$ " is

Application/Control Number: 10/584,076

Art Unit: 1624

deficient, see page 5, line 17.

Regarding claim 1, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention, see page 6, second to the last line. See MPEP § 2173.05(d).

Regarding claim 1, the phrase "or the like" renders the claim(s) indefinite because the claim(s) include(s) elements not actually disclosed (those encompassed by "or the like"), thereby rendering the scope of the claim(s) unascertainable, see page 6, last line. See MPEP § 2173.05(d).

Claim 2 recites the limitation "alkenyl" in the definition of R<sup>1</sup>. There is insufficient antecedent basis for this limitation in the claim.

Claims 3-5 recite the limitation "cyano" in the definition of R<sup>1</sup>. There is insufficient antecedent basis for this limitation in the claim.

Claim 8 recites the limitation "cycloalkyl" in the definition of R<sup>2</sup>. There is insufficient antecedent basis for this limitation in the claim.

Claim 10 recites the limitation "hydrogen" in the definition of R<sup>2</sup>. There is insufficient antecedent basis for this limitation in the claim.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or

Page 6

doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claims 29-31, 100 and 101 recite the broad recitation, followed by "in one embodiment" which is the narrower statement of the range/limitation.

Claims 32 and 33 recite the limitation " $NH_2$ " in the definition of  $R^{13}$ . There is insufficient antecedent basis for this limitation in the claim.

Claim 34 recites the limitation "alkyl, alkoxy,..., CONH-cycloalkyl, alkylsulfonyl, alkylsulfonylamino" in the definition of (CR<sup>9</sup>R<sup>10</sup>)<sub>w</sub>E. There is insufficient antecedent basis for these limitations in the claim.

Claim 50 is vague due to the reference to "Examples." Where are these examples? What are these examples? Thus, claim 50 is vague.

Claim 99 recite the limitation "NNCH<sub>2</sub>" in the definition of  $X^2$ . There is insufficient antecedent basis for this limitation in the claim.

Claim 102 recites the limitation "alkyl, alkoxy,..., CONH-cycloalkyl,..., alkylcarbonyl, dialkylcarbonyl, alkylcarbonylamino, alkoxycarbonyl, hydroxyalkyl, alkoxyalkyl, alkylcarbonyl-N(alkyl), cycloalkylaminocarbonyl, alkylaminocarbonyl, ..., dialkylaminoalkyl" in the definition of (CR<sup>9</sup>R<sup>10</sup>)<sub>w</sub>E. There is insufficient antecedent basis for these limitations in the claim.

Page 7

Art Unit: 1624

Claims 1-19, 21-27, 29-35, 50-53 and 95-103 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds of Formula 1, wherein X¹ and X²= single bond and only at the 4- and 7-position of the bicyclic pyrazolo[3,4-d]pyrimidines does not reasonably provide enablement for compounds of Formula 1, wherein X¹ is alkylene, -O-, -S-, -S(O)-, -SO<sub>2</sub>, -C(O)-, -CO(O)- or -C(O)NH- and X² is alkylene, -O-, -S-, -NH-, -N(C<sub>1-4</sub>alkyl), -NH-C<sub>1-4</sub>alkylene-, -N(C<sub>1-4</sub>alkyl)-C<sub>1-4</sub>alkylene-, -S(O)-, -SO<sub>2</sub>, -C(O)-, -CO(O)- or -C(O)NH- bonded anywhere on the bicyclic core with the other variables of formula (I) defined as in claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Pursuant to *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation is required: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue"; see *In re Vaeck*, 20 USPQ2d 1438, 1444.

# The analysis is as follows:

**(A) Breadth of claims: Scope of the compounds.** Owing to the range of many variables, trillions of substituted pyrazolo[3,4-d]pyrimidines are embraced.

- **(B) The nature of the invention:** The invention is a highly substituted pyrazolo[3,4-d]pyrimidines.
- **(C) Level of predictability in the art:** It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).
- (D) Direction or Guidance: That provided is very limited. Applicant shows a general synthesis of compounds of Formula 1, under Preparation on page 31 of the Specification, but does not show the starting material used to make the variety of compounds claimed. There is limited evidence in the Specification of the example compounds that only cover a small portion of the substituents claimed of Formula 1. Thus, there is no specific direction or guidance regarding said compounds of Formula 1 specifically mentioned in Scope.

The specification does not provide any support for the synthesis of compounds of Formula 1, wherein  $X^1$  is alkylene, -O-, -S-, -S(O)-, -SO<sub>2</sub>, -C(O)-, -CO(O)- or -C(O)NH- and  $X^2$  is alkylene, -O-, -S-, -NH-, -N(C<sub>1-4</sub>alkyl), -NH-C<sub>1-4</sub>alkylene-, -N(C<sub>1-4</sub>alkyl)-C<sub>1-4</sub>alkylene-, -S(O)-, -SO<sub>2</sub>, -C(O)-, -CO(O)- or -C(O)NH- bonded anywhere on the bicyclic core with the other variables of formula (I) defined as in claim 1. The availability of the

Page 9

Art Unit: 1624

starting material that is needed to prepare the invention as claimed is at issue here...As per MPEP 21'64.01 (b). A key issue that can arise when determining whether the specification is enabling is whether the starting materials or apparatus necessary to a make the invention are available. In the biotechnical area, this is often true when the product or process requires a particular strain of microorganism and when the microorganism is available only after extensive screening. The Court in *In re Ghiron*, 442 F.2d 985, 991,169 USPQ 723, 727 (CCPA 1971), made it clear that if the practice of a method requires a particular apparatus, the application must provide a sufficient disclosure of the apparatus if the apparatus is not readily available. The same can be said if certain chemicals are required to make a compound or practice a chemical process. *In re Howarth*, 654 F.2d 103, 105, 210 USPQ 689, 691 (CCPA 1981).

**(E) State of the Prior Art:** These compounds are substituted pyrazolo[3,4-d]pyrimidines of Formula I wherein  $X^1$  and  $X^2$ = single bond and only at the 4- and 7-position of the bicyclic pyrazolo[3,4-d]pyrimidines, which are well documented in the art. So far as the examiner is aware, no substituted pyrazolo[3,4-d]pyrimidines of Formula I wherein wherein  $X^1$  is alkylene, -O-, -S-, -S(O)-, -SO<sub>2</sub>, -C(O)-, -CO(O)- or -C(O)NH- and  $X^2$  is alkylene, -O-, -S-, -NH-, -N(C<sub>1-4</sub>alkyl), -NH-C<sub>1-4</sub>alkylene-, -N(C<sub>1-4</sub>alkyl)-C<sub>1-4</sub>alkylene-, -S(O)-, -SO<sub>2</sub>, -C(O)-, -CO(O)- or -C(O)NH- bonded anywhere on the bicyclic core and with the other variables of formula (I) defined as in claim 1 of any have been made or used.

Application/Control Number: 10/584,076 Page 10

Art Unit: 1624

**(F) Working Examples:** Applicant shows examples 1-11 on pages 53, 55 and 56 but no working examples were shown of Formula I wherein  $X^1$  is alkylene, -O-, -S-, -S(O)-, -SO<sub>2</sub>, -C(O)-, -CO(O)- or -C(O)NH- and  $X^2$  is alkylene, -O-, -S-, -NH-, -N(C<sub>1-4</sub>alkyl), -NH-C<sub>1-4</sub>alkylene-, -N(C<sub>1-4</sub>alkyl)-C<sub>1-4</sub>alkylene-, -S(O)-, -SO<sub>2</sub>, -C(O)-, -CO(O)- or -C(O)NH- bonded anywhere on the bicyclic core with the other variables of formula (I) defined as in claim 1.

- **(G) Skill of those in the art:** The ordinary artisan is highly skilled.
- **(H)** The quantity of experimentation needed: Since there are very limited working examples as described above, the amount of experimentation is expected to be high and burdensome.

Due to the level of unpredictability in the art, the very limited guidance provide, and the lack of working examples, the Applicant has shown lack of enablement for the groups noted groups on Formula i. MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

# Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

- 1. Determining the scope and contents of the prior art.
- 2. Ascertaining the differences between the prior art and the claims at issue.
- 3. Resolving the level of ordinary skill in the pertinent art.
- 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-12, 14, 16, 18-42, 50-53 and 95-103 are rejected under 35 U.S.C. 103(a) as being unpatentable over Faraci et. al. (US 6103900).

The instant Application claims compounds of formula (I), wherein  $X^1$  and  $X^2$ = bond, A=5-methylthio-pyrazolo[3,4-d]pyrimidine with  $X^1$  and  $X^2$  bonded at the 4- and

Application/Control Number: 10/584,076

Art Unit: 1624

7-position of the bicycle, D= 2,6-dichloro-4-trifluoromethylphenyl,  $R^1$ = 2-chloro, n= 2,  $R^2$ = 4-trifluoromethyl,  $R^2$ = 6-chloro, Y- $R^3$ = 5-S(O)<sub>2</sub>NH<sub>2</sub> and compositions thereof.

Faraci et. al. teaches compounds of formula (I), wherein  $X^1$  and  $X^2$ = bond, A= 5-methylthio-pyrazolo[3,4-d]pyrimidine with  $X^1$  and  $X^2$  bonded at the 4- and 7-position of the bicycle, D= 2,6-dichloro-4-trifluoromethylphenyl,  $R^1$ = 2-chloro, n= 2,  $R^2$ = 4-trifluoromethyl,  $R^2$ = 6-chloro, Y- $R^3$ = hydrogen at the 5-position of the bicycle. See column 35, the third compound listed in the table.

The difference between the reference and the instant Application is the substitution on at the 5-position of the phenyl ring, hydrogen versus Applicant's  $S(O)_2NH_2$ . The genus in the reference in colum 1, lines 40-50 and in column 2, lines 17-26, teaches that hydrogen and the  $S(O)_2NH_2$  are alternatively useable. See "may be substituted" in column 2, line 17 and the list of substituents that follow in lines 20-26, embrace the  $R^1$ ,  $R^2$  and Y- $R^3$  substituents on the phenyl, which states the following:

above groups may be substituted independently by from one to three of fluoro, chloro, bromo,  $C_1$ – $C_6$  alkyl,  $C_1$ – $C_6$  alkoxy, or trifluoromethyl, or one of cyano, nitro, amino, NH( $C_1$ – $C_6$  alkyl), N( $C_1$ – $C_4$  alkyl)( $C_1$ – $C_2$  alkyl), COO ( $C_1$ – $C_4$  alkyl), CO( $C_1$ – $C_4$  alkyl), SO<sub>2</sub>NH( $C_1$ – $C_4$  alkyl), SO<sub>2</sub>NH<sub>2</sub>, NHSO<sub>2</sub>( $C_1$ – $C_4$  alkyl), S( $C_1$ – $C_6$  alkyl), SO<sub>2</sub>( $C_1$ – $C_6$  alkyl), wherein said  $C_1$ – $C_4$  alkyl and  $C_1$ – $C_6$  alkyl may be substituted by one or two of fluoro, chloro, hydroxy, amino, methylamino, dim-

ethylamino or acetyl;

as indicated above. Furthermore, the A substituent maybe further substituted according to the genus in the reference in column 1, lines 54-61,

which may be substituted by  $R_6$  which is hydrogen,  $C_1-C_6$  alkyl, fluoro, chloro, bromo, hydroxy, amino,  $O(C_1-C_6)$ : alkyl,  $NH(C_1-C_6)$  alkyl,  $N(C_1-C_6)$  alkyl,  $N(C_1-C_6)$  alkyl,  $N(C_1-C_6)$  alkyl,  $N(C_1-C_6)$  alkyl, wherein n=0,1 or 2, wherein said  $N(C_1-C_6)$  alkyl may be substituted by from 1 to 3 substituents  $N(C_1-C_6)$  alkyl may be substituted by from 1 to 3 substituents  $N(C_1-C_6)$  alkyl may be substituted by from 1 to 3 substituents  $N(C_1-C_6)$  alkyl may be substituted by from 1 to 3 substituents  $N(C_1-C_6)$  alkyl may be substituted by from 1 to 3 substituents  $N(C_1-C_6)$  alkyl may be substituted by from 1 to 3 substituents  $N(C_1-C_6)$  alkyl may be substituted by from 1 to 3 substituents  $N(C_1-C_6)$  alkyl may be substituted by from 1 to 3 substituents  $N(C_1-C_6)$  alkyl may be substituted by from 1 to 3 substituents  $N(C_1-C_6)$  alkyl may be substituted by from 1 to 3 substituents  $N(C_1-C_6)$  alkyl may be substituted by from 1 to 3 substituents  $N(C_1-C_6)$  alkyl may be substituted by from 1 to 3 substituents  $N(C_1-C_6)$  alkyl may be substituted by from 1 to 3 substituents  $N(C_1-C_6)$  alkyl may be substituted by from 1 to 3 substituents  $N(C_1-C_6)$  alkyl may be substituted by from 1 to 3 substituents  $N(C_1-C_6)$  alkyl may be substituted by from 1 to 3 substituents  $N(C_1-C_6)$  alkyl may be substituted by from 1 to 3 substituents  $N(C_1-C_6)$  alkyl may be substituted by from 1 to 3 substituents  $N(C_1-C_6)$  alkyl may be substituted by from 1 to 3 substituents  $N(C_1-C_6)$  alkyl may be substituted by from 1 to 3 substituents  $N(C_1-C_6)$  alkyl may be substituted by from 1 to 3 substituents  $N(C_1-C_6)$  alkyl may be substituted by from 1 to 3 substituted by f

as indicated above for R<sup>13</sup>. Furthermore, the D substituent maybe aryl or heteroaryl, i.e. thiazolyl, as indicated by column 2, lines 27-35 and further substituted according to the genus in the reference in column 2, lines 54-61,

phenyimethyl, wherein each of the above groups may be substituted independently by from one to three of fluoro, chloro, bromo, trifluoromethyl,  $C_1-C_5$  alkyl or  $C_1-C_5$  alkoxy, or one of cyano, nitro, amino,  $NH(C_1-C_5$  alkyl),  $N(C_2-C_4$  alkyl)( $C_1-C_2$  alkyl),  $CO(C_1-C_4$  alkyl),  $CO(C_1-C_4$  alkyl),  $SO_2NH(C_1-C_4$  alkyl),  $SO_2N(C_2-C_4$  alkyl),  $SO_2NH_2$ ,  $NH_2SO_2(C_1-C_4$  alkyl),  $S(C_1-C_5$  alkyl),  $SO_2(C_1-C_6$  alkyl), wherein said  $C_1-C_4$ 

As indicated above for  $((CR^9R^{10})_wE)_k$ . Furthermore, if D is substituted anywhere on the pyrimidine, then  $X^2$ -D could be  $R_6$  from the reference. Moreover,  $R_6$  is defined as  $X^2 = S(O)_n$  or NH and D=  $(C_1$ -C<sub>6</sub>alkyl), see column 1, lines 56-57.

The compositions are found in column 14, lines 30-32.

Thus, said claims are rendered obvious by Faraci et. al.

#### Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUSANNA MOORE whose telephone number is (571)272-9046. The examiner can normally be reached on M-F 8:00-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Susanna Moore/ Examiner, Art Unit 1624

/Brenda L. Coleman/ Primary Examiner, Art Unit 1624